REMARKS

Claims 7-9 and 20-25 are pending, and all claims were rejected. Claim 7 is amended herein. Support for the amendment is found at page 61, lines 20-26. Although this amendment is proposed after a final rejection, it is respectfully submitted that entry advances prosecution by placing the claims in a better position for allowance and appeal.

Applicants gratefully acknowledge that claim 10 is properly viewed as in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph. Applicants appreciate the withdrawal of this rejection as well as the withdrawal of the objections by the Examiner.

Rejection Under 35 U.S.C. §§ 101 and 112, First Paragraph

Claims 7-9 and 20-25 are rejected under 35 U.S.C. §§ 101 and 112, first paragraph as allegedly lacking either a credible, specific and substantial asserted utility or a well established utility. According to the Action, the structural similarity among small soluble proteins such as cytokines is not predictive of functional similarity. The Action asserts that the Kumar *et al.* reference describes a utility for IL-1ε and not IL-1δ. The Action also states that while Debets *et al.* demonstrates the upregulation of IL-1δ in psoriasis, this is insufficient because psoriasis is not specifically mentioned in the specification as filed. According to the Action, chromosomal mapping, tissue distribution, IL-1 receptor binding activity, IL-1 receptor antagonist activity, participation in inflammation or other immunological disorders, and the identification of novel IL-1 receptors are not substantial, specific, and credible utilities. Finally, the Action reasserts the applicability of earlier cited references as supporting the Office's position of an absence of utility for the claimed invention. Applicants respectfully traverse this rejection.

Applicants acknowledge that Kumar *et al.* describes the role of IL-1ε, and not IL-1δ, in viral infections. *See* Kumar *et al.*, *J. Biol. Chem.*, 275: 10308-14 (2000). Nonetheless, Applicants believe that the findings of Kumar *et al.* further provide support for a utility of IL-1δ for the reasons discussed below.

Applicants respectfully submit that the specification as filed sets forth at least one specific and substantial utility sufficient to satisfy 35 U.S.C. §§ 101 and 112. For example, the specification discloses IL-1δ is involved in inflammation, a specific and substantial utility. Contrary to the assertion of the Office, inflammation is not a general term for a diverse set of diseases. Rather, it describes a complex, but predictable response that includes defined cytokines (*e.g.*, IL-1, TNF-α), cellular components (*e.g.*, neutrophils, lymphocytes), and other soluble mediators (*e.g.*, platelets) that interact to induce vascular permeability, cellular extravasation into tissue, and activation of the tissue-recruited cells. *See, e.g.,* Exhibits A, at page 36-37, Exhibit B, at page 1051-52. The diversity of the resulting disease states is specific to the organ system in which the inflammation occurs, not the initiating inflammatory process. The cascade of events described as "inflammation" is defined and well known as a biological process with common characteristics regardless of the organ system in which inflammation occurs. Therefore, Applicants assert that inflammation qualifies as a specific process.

The evidence of IL-1δ's role in inflammation is at least three-fold. First, Debets *et al.* demonstrates the induction of IL-1δ expression in keratinocytes after stimulation by the classical pro-inflammatory cytokines of IL-1β and TNF-α and in activated macrophages (a key mediator of inflammation). *See* Debets *et al.*, *J. Immunol.*, 167: 1440, 1442-44, Figures 3 and 6 (2001). Second, IL-1δ is overexpressed in psoriatic skin lesions. *See* Debets, at pages 1443-44 and Figure 6. Psoriasis is a skin disease characterized by inflammation. *See, e.g.,* Exhibit C. Therefore, the overexpression of IL-1δ in clinical psoriatic lesions is understood by a skilled artisan to implicate the cytokine in the observed inflammation. Third, IL-1δ is a member of the IL-1 family of cytokines as identified by structural and sequence similarity disclosed in the specification. *See, e.g.,* specification at page 79, lines 26-29. The structural and sequence similarity to other members of the IL-1 family support Applicants' assertion of IL-1δ's utility. To date, unlike many of structurally related cytokine families, all of the members of the IL-1 family possess a common β-barrel structure, and every member functionally characterized is

involved in inflammatory signaling. The specification states that the family of IL-1 cytokines is involved in a broad range of biological functions and "typically affect similar immune functions, including inflammatory responses." *See* specification, at page 31, lines 33-35. Therefore, it would be credible or believable to a person of skill in the art that other IL-1 family members would also function in inflammation as disclosed in the specification.

The specification also discloses IL-1δ's utility as a modulator of immune function and as a cytokine involved in viral infections and immunological disorders. *See* specification at page 79, line 26 to page 81, line 11. The previously submitted, post-filing references provide support for these specific and substantial utilities. First, Debets *et al.* demonstrates that IL-1δ acts as a specific and potent antagonist of IL-1ε. *See* Debets, at page 1443. As an antagonist of an IL-1 family member, IL-1δ has utility in modulating the immune response mediated by IL-1ε. Second, Kumar *et al.* establishes IL-1ε is expressed *in vivo* in response to a viral infection (*i.e.*, herpes simplex virus) (as acknowledged by the Office) and in a murine model of skin inflammation (*i.e.*, chronic oxazolone-mediated contact hypersensitivity). *See* Kumar, at page 10312-13 and Figures 4 and 5. In other words, IL-1ε functions similarly to other characterized IL-1 family members, namely IL-1α and IL-1β, in its involvement in viral response and inflammation. IL-1δ also functions similarly to other characterized IL-1 family members, namely IL-1ra, as a modulator of a particular IL-1 family member's function, *i.e.*, IL-1ε. Therefore, these references support the disclosed utility for IL-1δ as a modulator of inflammation in viral infections and immunological disorders.

Taken together, the specification discloses IL-1δ as having a specific and substantial utility in inflammation, infectious disease, and other immunological disorders. The data summarized above demonstrates IL-1δ expression *in vitro* with pro-inflammatory cytokine treatment and *in vivo* expression in inflammatory lesions (*i.e.*, psoriatic lesions) as well as IL-1δ's potent effects as an antagonist of IL-1ε, a cytokine expressed in viral infections (*i.e.*, HSV) and in models of immunological disorders (*i.e.*, contact hypersensitivity/allergy).

Finally, the utilities disclosed in the specification are credible to one of skill in the art. Textbooks relied upon by skilled artisans treat inflammation as a specific and distinct biologic process. *See* Exhibits A and B. The shared structural features and uniform participation in a specific process (*i.e.*, inflammation) is sufficient for a skilled artisan to recognize and believe the disclosed utilities. Thus, the utility standard set forth under 35 U.S.C. §§ 101 and 112 is met by the instant disclosure.

Claim 7 was rejected by the Office, and Applicants have amended claim 7 to clarify the binding site for the claimed binding compound as an epitope located within the claimed contiguous amino acid residues.

In light of the above remarks, Applicants respectfully submit that the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, are overcome. Therefore, Applicants request the withdrawal of the rejections.

CONCLUSION

Applicants submit that the rejections under 35 U.S.C. §§ 101 and 112 have been overcome by the above remarks. Early allowance of pending claims 7-9 and 20-25 is respectfully requested. If the Examiner feels that a telephonic conference would be helpful, please call the undersigned at 858-720-7955 at your convenience.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 140942000310.

Respectfully submitted,

Dated: February 3, 2003

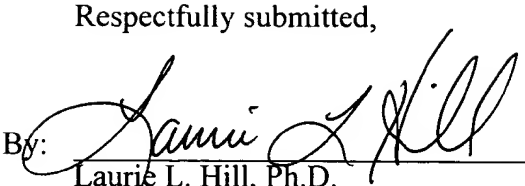
By: 

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EXHIBIT D

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Please amend claim 7 as follows:

7. (Twice Amended) A binding compound comprising an antigen binding site from an antibody, which specifically binds to a mature polypeptide comprising at least 8 contiguous amino acid residues from SEQ ID NO:2, wherein said antigen binding site specifically binds an epitope located within said contiguous amino acid residues.

1: Am J Health Syst Pharm 2000 Apr 1;57(7):645-59; quiz 660-1

Pathophysiology and treatment of psoriasis.

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The pathogenesis and treatment of psoriasis are reviewed. Psoriasis is characterized by defects in the normal cycle of epidermal development that lead to epidermal hyperproliferation, altered maturation of skin cells, and vascular changes and inflammation. The condition typically manifests as areas of thickened, flaky, silvery white and reddened skin that may hurt, itch, and bleed. Biochemical markers of psoriasis are changes in levels of keratins, keratinocyte transglutamase, migration inhibitory factor-related protein, skin-derived antileukoproteinase, involucrin, small protein rich protein 2, filaggrin, and cytokines. Types of psoriasis that may be clinically encountered include plaque psoriasis, guttate psoriasis, erythrodermic psoriasis, and pustular psoriasis. Psoriasis is believed to be genetically linked but can also be triggered by mechanical, ultraviolet, and chemical injury; various infections; prescription drug use; psychological stress; smoking; and other factors. Topical treatment of psoriasis is usually the first line of therapy. Topical treatments consist of emollients and keratolytic agents, anthralin, coal tar, corticosteroids, vitamin D3 analogues, topical retinoids, and topical psoralens plus ultraviolet A (UVA) light. In patients who do not respond adequately to topical therapy, oral or injectable therapy, such as oral retinoids, methotrexate, cyclosporine, tacrolimus, and oral psoralens plus UVA light, may be warranted. Patients receiving systemic

treatments should be carefully monitored for adverse effects and drug-drug interactions. Drug therapy is the mainstay of the treatment of psoriasis. The potential adverse effects and interactions necessitate vigilant monitoring.

Publication Types:

- Review
- Review, Tutorial

PMID: 10768819 [PubMed - indexed for MEDLINE]
